# KB-R7943 mesylate

**Cat. No.:** HY-15415

**CAS No.:** 182004-65-5

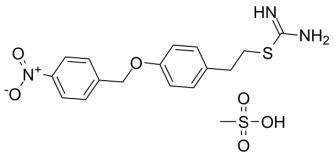
**Molecular Formula:** $C_{17}H_{21}N_3O_6S_2$

**Molecular Weight:** 427.5

**Target:** Na+/Ca2+ Exchanger; Autophagy

**Pathway:** Membrane Transporter/Ion Channel; Autophagy

**Storage:** 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 100 mg/mL (233.92 mM; Need ultrasonic)

| Preparing Stock Solutions | Concentration / Solvent / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.3392 mL | 11.6959 mL | 23.3918 mL |
| | 5 mM | 0.4678 mL | 2.3392 mL | 4.6784 mL |
| | 10 mM | 0.2339 mL | 1.1696 mL | 2.3392 mL |

Please refer to the solubility information to select the appropriate solvent.

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.85 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.85 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.85 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

KB-R7943 mesylate is a widely used inhibitor of the reverse $Na^+/Ca^{2+}$ exchanger ($NCX_{rev}$) with $IC_{50}$ of 5.7±2.1 μM. KB-R7943 mesylate induces cancer cell death via activating the JNK pathway and blocking autophagic flux.

**$IC_{50}$ & Target**

IC50: 5.7±2.1 μM ($Na^+/Ca^{2+}$ exchanger)[1]

**In Vitro**

KB-R7943 mesylate blocks NMDAR-mediated ion currents, and inhibits NMDA-induced increase in cytosolic $Ca^{2+}$ with $IC_{50}$ =13.4±3.6 μM but accelerates calcium deregulation and mitochondrial depolarization in glutamate-treated neurons. KB-R7943 depolarizes mitochondria in a $Ca^{2+}$-independent manner. KB-R7943 inhibits 2,4-dinitrophenol-stimulated respiration of cultured neurons with $IC_{50}$=11.4±2.4 μM. In addition to $NCX_{rev}$, KB-R7943 dose-dependently and reversibly blocked ion

currents elicited by NMDA. KB-R7943 dose-dependently inhibits NMDA-induced increases in $[Ca^{2+}]_c$ with $IC_{50}$=13.4±3.6 μM confirming the inhibition of NMDA receptors observed in electrophysiological experiments[1]. $_{wt}$RyR1-HEK 293 pretreated with KB-R7943 (10 μM, 10 min) dissolved in the bulk perfusion exhibited significantly attenuated responses to caffeine. In this regard, KB-R7943 produced more pronounced inhibition of caffeine-induced $Ca^{2+}$ release elicited by 1 mM compared with 0.5 and 0.75 mM (60 versus 58 versus 37%, p<0.05, respectively)[2]. KB-R7943 inhibits both $I_{hERG}$ and native $I_{Kr}$ rapidly on membrane depolarization with $IC_{50}$ values of ~89 and ~120 nM, respectively, for current tails at −40 mV following depolarizing voltage commands to +20 mV. $I_{hERG}$ inhibition by KB-R7943 exhibits both time- and voltage-dependence but shows no preference for inactivated over activated channels[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

**Cell Assay** [2]

EK 293 cells stably expressing the $_{wt}$RyR1 ($_{wt}$RyR1-HEK 293) are maintained in Dulbecco's modified Eagle's medium supplemented with 2 mM glutamine, 100 μg/mL streptomycin, 100 U/mL penicillin, 1 mM sodium pyruvate, and 10% fetal bovine serum at 37°C under 5% $CO_2$. $_{wt}$RyR1-HEK 293 cells are loaded with 5 μM Fluo-4 acetoxymethyl ester at 37°C for 30 min to measure $Ca^{2+}$ transients in an imaging buffer consisting of 140 mM NaCl, 5 mM KCl, 2 mM $MgCl_2$, 2 mM $CaCl_2$, 10 mM HEPES, and 10 mM glucose, pH 7.4, supplemented with 0.05% bovine serum albumin. The cells are washed three times with imaging buffer and additionally incubated for 20 min at room temperature. Dye-loaded cells are washed three times with imaging buffer and imaged with a charge-coupled device camera with a 40× objective lens attached to an IX-71 microscope. The sequence of images is captured and monitored using EasyRatioPro. Caffeine dissolved in the imaging buffer is focally applied for 15 s using AutoMate Scientific. KB-R7943 is dissolved in the imaging buffer, and $_{wt}$RyR1-HEK 293 cells are incubated for 10 min before the application of caffeine[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Br J Pharmacol. 2021 Apr 22.
- Aging Cell. 2022 May;21(5):e13593.
- J Am Heart Assoc. 2022 Jul 29;e025328.

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## REFERENCES


[1]. Brustovetsky T, et al. KB-R7943, an inhibitor of the reverse Na+ /Ca2+ exchanger, blocks N-methyl-D-aspartate receptor and inhibits mitochondrial complex I. Br J Pharmacol. 2011 Jan;162(1):255-70.

[2]. Barrientos G, et al. The Na+/Ca2+ exchange inhibitor 2-(2-(4-(4-nitrobenzyloxy)phenyl)ethyl)isothiourea methanesulfonate(KB-R7943) also blocks ryanodine receptors type 1 (RyR1) and type 2 (RyR2) channels. Mol Pharmacol. 2009 Sep;76(3):560-8.

[3]. Cheng H, et al. High potency inhibition of hERG potassium channels by the sodium-calcium exchange inhibitor KB-R7943. Br J Pharmacol. 2012 Apr;165(7):2260-73.

[4]. Long Z, et al. The reverse-mode NCX1 activity inhibitor KB-R7943 promotes prostate cancer cell death by activating the JNK pathway and blocking autophagic flux. Oncotarget. 2016;7(27):42059-70.

**Caution: Product has not been fully validated for medical applications. For research use only.**

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